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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,534	01/25/2001	Paul D. Coleman	12610-003002	6783

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EXAMINER
SAKELARIS, SALLY A

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/15/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/770,534	COLEMAN ET AL.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-75,87-92 and 99* is/are pending in the application.

4a) Of the above claim(s) *76-86,93-98 and 100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-75,87-92 and 99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Response to Arguments

Applicant's election without traverse of Group I, claims 57-65, 73-75, 87, 88, 90-92, and 99, drawn to a method for creating a gene profile in paper No. 10, filed 09-20-2002 is acknowledged.

Specification

Additionally, the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, as seen for example on page 25. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Priority

Acknowledgement of the now abandoned, parent application, 09/178,170 filed 10/23/1998 and of the provisional application 60/063,274 filed 10/24/1997 from which it claims benefit has been made. The filing date of the instant claims is deemed to be the filing date of the present application, 01/25/2001(Please see new matter rejection below for explanation).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 57-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Allen et al. (Neuroscience Letters, 1991).

Allen et al. teach a method for creating a gene profile for a given stage of Alzheimer's disease by providing a plurality of "mRNAs found in a variety of extraneural tissues... because a hematogenous source for abnormal amyloid deposits is possible in AD"(Allen, 109). The reference teaches that forms of mRNA are present in human serum, plasma and platelets and often even in the cerebral vasculature. Determination of the level of mRNA expression is undertaken through either a method synthesizing cDNA by reverse transcription, or in the case of some peripheral tissues, a RT-PCR method was employed. The reference teaches that the expression of mRNAs in AD-affected peripheral mononuclear blood cells(PMBCs), is relevant developmentally as they "give rise to microglia, which are often seen in proximity to Beta Amyloid Precursor Protein(BAPP) deposits"(109) eventually in the AD brain. The reference aptly teaches the detection of mRNA precursors to known components of the AD brain, as AD is a progressive neurodegenerative disorder characterized by abnormal deposition of the Beta amyloid protein(BAP).

2. Claims 57-59, 65, 73, 87, 88, 90, and 99 are rejected under 35 U.S.C. 102(b) as being anticipated by Markham et al.(US 5,952,481).

Markham et al. teach creating a gene profile for a given stage of Alzheimer's disease(Col.24), providing a plurality of cells from non-neural tissue or bodily fluid of a patient who has Alzheimer's disease(Col.24 lines,33-38). The patent further teaches the isolation of heterologous mRNA from the plurality of isolated peripheral white blood cells, and the mRNA's subsequent copying into single stranded cDNA using oligo-dT as a primer and, for example,

reverse transcriptase. Markham also teaches that alternative methods of mRNA analysis in patient samples can be used in the practice of the invention. For example, the technique of RT-PCR may be applied. Also Markham et al. teach the hybridization and detection of polynucleotides such as those polynucleotides that encode genes that have been said to play a role in "G1-S cell cycle progression and G2 check point progression"(Col.6, lines 27-29). It is important to note that the patent teaches practicing the method using a sample containing polynucleotides from any peripheral white blood cell(Col.24, lines 34-35). Furthermore, the reference teaches normal data which allows for the identification of variations within the class of human genes being isolated and as a result, aid in the diagnosis of degenerative diseases such as familial AD and/or sporadic AD. The Markham reference teaches a "method which enables a determination of a predisposition for and diagnosis of degenerative diseases such as AD, as well as products and processes for treating and obtaining treatments for a degenerative disease such as AD"(Col.8, lines 16-20).

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

3. Claims 57-59, 65, 73-75, 87, 88, 90, 91, 92, and 99 are rejected under 35 U.S.C. 102(e) as being anticipated by Au-Young et al. (US Patent 6,500,938 B1)

Au-Young et al. teach creating a gene profile for a given stage of Alzheimer's disease(Col.11, lines 15-20 & Col.12, lines 32-35), providing a plurality of cells from non-neural tissue or bodily fluid of a patient who has Alzheimer's disease(Col. 8, lines 5-10 & Col.11, lines 44-49). The patent further teaches the isolation of heterologous mRNA from any of the aforementioned plurality of cells(Col.8 lines 5-10), and its subsequent reverse transcription in the presence of quantitation controls within the sample to assure that amplification and labeling procedures do not change the true distribution of target polynucleotides in a sample(Col. 8 lines 36-50). Also Au-Young et al. teach the hybridization and detection of polynucleotides such as those mRNAs encoding cell cycle regulators(Table 1 SEQ ID NO:1382)in a cDNA micro-array analysis(Col. 11, lines 36-43). It is important to note that the patent teaches practicing the method using a sample containing polynucleotides from "any bodily fluid(blood, urine, saliva, phlegm, gastric juices, etc.), cultured cells, biopsies, or other tissue preparations"(Col. 8, lines 5-9). Furthermore, the reference teaches the use of the micro-array in monitoring the progression of disease as "researchers can assess and catalog the differences in gene expression between healthy and diseased tissues or cells. By analyzing changes in patterns of gene expression, disease can be diagnosed at earlier stages before the patient is symptomatic"(Col.11, lines 44-49). Lastly, Au-Young et al, teaches the method of using their "invention to rapidly screen large numbers of candidate drugs, looking for ones that have an expression profile similar to those of known therapeutic drugs, with the expectation that molecules with the same expression profile

will likely have similar therapeutic effects, thus providing the means to determine the molecular mode of action of a drug"(Col.12, lines 52-58).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al.(Neuroscience Letters, 1991) in view of Ikeda et al. (Human Pathology, 1990).

Allen et al. teach a method for creating a gene profile for a given stage of Alzheimer's disease by providing a plurality of "mRNAs found in a variety of extraneural tissues... because a hematogenous source for abnormal amyloid deposits is possible in AD"(Allen, 109). The reference teaches that forms of mRNA are present in human serum, plasma and platelets and often even in the cerebral vasculature. Determination of the level of mRNA expression is undertaken through either a method synthesizing cDNA by reverse transcription, or in the case of some peripheral tissues, a RT-PCR method was employed. The reference teaches that the expression of mRNAs in AD-affected peripheral mononuclear blood cells(PMBCs), is relevant developmentally as they "give rise to microglia, which are often seen in proximity to Beta Amyloid Precursor Protein(BAPP) deposits"(109) eventually in the AD brain. The reference aptly teaches the detection of mRNA precursors to known components of the AD brain, as AD is

a progressive neurodegenerative disorder characterized by abnormal deposition of the Beta amyloid protein(BAP).

Allen et al. do not teach obtaining neuronal cells and viewing NFTs through a microscope to determine if the cells are filled with neurofibrillary tangles(NFT) that are not frank.

However, Ikeda et al. teach microscopic examination of "case no.1" that revealed a decreased number of neurons with a diffuse distribution of senile plaques and neurofibrillary tangles(NFTs). The abundance of NFTs in the brain of case no. 1 is "consistent with a diagnosis of AD...furthermore, on the basis of all the clinical and pathologic information, this case is considered to be AD at an advanced stage"(1224). Case 2 represented an example of an early stage of AD(probable familial)"Additionally, a very small number of neurofibrillary tangles was seen in the neocortical sections, but the diencephalons and cerebellum did not show any significant lesions"(1223) in "case no.2". The reference teaches that "these findings suggest that case no. 2 might be an example of AD at a very early stage, with pathologic changes that would eventually develop into a picture similar to that of case no.1 with advanced AD having many typical or classical senile plaques"(1224).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Allen et al. so as to have provided an additional process for the detection or diagnosis of Alzheimer's involving observing NFT, in a stage-dependent configuration, under the microscope.

5. Claims 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young et al.(US 6,500,938 B1) in view of Mercken et al. (US 6,238,892).

Au-Young et al. teach creating a gene profile for a given stage of Alzheimer's disease(Col.11, lines 15-20 & Col.12, lines 32-35), providing a plurality of cells from non-neural tissue or bodily fluid of a patient who has Alzheimer's disease(Col. 8, lines 5-10 & Col.11, lines 44-49). The patent further teaches the isolation of heterologous mRNA from any of the aforementioned plurality of cells(Col.8 lines 5-10), and its subsequent reverse transcription in the presence of quantitation controls within the sample to assure that amplification and labeling procedures do not change the true distribution of target polynucleotides in a sample(Col. 8 lines 36-50). Also Au-Young et al. teach the hybridization and detection of polynucleotides such as those mRNAs encoding cell cycle regulators(Table 1 SEQ ID NO:1382)in a cDNA micro-array analysis(Col. 11, lines 36-43). It is important to note that the patent teaches practicing the method using a sample containing polynucleotides from "any bodily fluid(blood, urine, saliva, phlegm, gastric juices, etc.), cultured cells, biopsies, or other tissue preparations"(Col. 8, lines 5-9). Furthermore, the reference teaches the use of the micro-array in monitoring the progression of disease as "researchers can assess and catalog the differences in gene expression between healthy and diseased tissues or cells. By analyzing changes in patterns of gene expression, disease can be diagnosed at earlier stages before the patient is symptomatic"(Col.11, lines 44-49). Lastly Au-Young et al, teaches the method of using their "invention to rapidly screen large numbers of candidate drugs, looking for ones that have an expression profile similar to those of known therapeutic drugs, with the expectation that molecules with the same expression profile

will likely have similar therapeutic effects, thus providing the means to determine the molecular mode of action of a drug"(Col.12, lines 52-58).

Au-Young et al. do not teach viewing neuronal cells that lack frank neurofibrillary tangles(NFT) under the microscope.

However, Mercken et al. teach monoclonal antibodies, specifically "AT8", "does not decorate any normal structures but only produces abundant staining of NFT...Some apparently tangle free neurons were diffusely stained, often exhibiting a strong perinuclear staining"(FIG. 3, Col. 13) Mercken et al. thus teach microscopy(Col. 13 line 13)with the ability to discern a stage of Alzheimer's in AT8's preferential staining of the frank neurofibrillary tangles characteristic to Alzheimer disease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Au-Young et al. so as to have provided an additional process for the detection or diagnosis of a brain disease involving observing the presence or absence of NFT under the microscope Alzheimer's disease(Col. 7, lines 53-56).

6. Claims 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Markham et al.(US 5,952,481) in view of Callahan et al. (Neurobiology of Aging, 1994) and in further view of Ghanbari et al. (US 5,811,310).

Markham et al. teach creating a gene profile for a given stage of Alzheimer's disease(Col.24), providing a plurality of cells from non-neural tissue or bodily fluid of a patient who has Alzheimer's disease(Col.24 lines,33-38). The patent further teaches the isolation of heterologous mRNA from the plurality of isolated peripheral white blood cells, and the mRNA's subsequent copying into single stranded cDNA using oligo-dT as a primer and, for example,

reverse transcriptase. Markham also teaches that alternative methods of mRNA analysis in patient samples can be used in the practice of the invention. For example, the technique of RT-PCR may be applied. Also Markham et al. teach the hybridization and detection of polynucleotides such as those polynucleotides that encode genes that have been said to play a role in "G1-S cell cycle progression and G2 check point progression"(Col.6, lines 27-29). It is important to note that the patent teaches practicing the method using a sample containing polynucleotides from any peripheral white blood cell(Col.24, lines 34-35). Furthermore, the reference teaches normal data which allows for the identification of variations within the class of human genes being isolated and as a result, aid in the diagnosis of degenerative diseases such as familial AD and/or sporadic AD. The Markham reference teaches a "method which enables a determination of a predisposition for and diagnosis of degenerative diseases such as AD, as well as products and processes for treating and obtaining treatments for a degenerative disease such as AD"(Col.8, lines 16-20).

Markham et al. do not teach determining the stage of Alzheimer's by obtaining neuronal cells and exposing at least one of the neuronal cells to two or more antibodies wherein the antibodies comprise: an anti-TG-3 and mAb69; or an anti-MC-1 and mAb69.

However, Callahan et al. does teach determining the stage of Alzheimer's by obtaining neuronal cells and exposing them to two or more antibodies wherein the antibodies comprise: mAb69 and biotinylated horse antimouse(382). Callahan et al. further teach that "end-stage Alzheimer's disease cases demonstrated sparse grain density for GAP-43 probe over tangle-bearing neurons"(Fig. 1a and b). While in neurons partially filled with NFT, "grains appeared to be equally probably over NFT vs. over NFT-free regions of the cell"(Fig 1c). The reference

teaches the use of mAb69 as a marker of frank NFT formation as seen in for example in Fig.1 when "parahippocampal gyrus sections reacted with mAb69 for PHF-tau", a conformational epitope in NFT(383).

Callahan et al. do not teach determining the stage of Alzheimer's by obtaining neuronal cells and exposing at least one of the neuronal cells to two or more antibodies wherein the antibodies comprise: an anti-TG-3 and mAb69; or an anti-MC-1 and mAb69 together.

However, Ghanbari et al. teach the use of an antibody, ALZ-50, whose action is analogous to that of mAb69 and whose action is taught to be coupled with the use of the claimed MC-1 and TG3. Ghanbari et al. teach that ALZ-50 reacts with normal and recombinant(abnormally phosphorylated) Tau from human origin. As is well known in the art, Ghanbari et al teach several antibodies that show reactivity to human tau either through non-specific cross-reactions with normal and abnormally phosphorylated tau or because they recognized specific epitopes on normal and abnormal phosphorylated tau. Ghanbari also reiterates that in the art many antibodies to specific phosphorylation sites and conformations of tau have been combined in double immunocytochemistry(ICC) experiments. It is further typical that in the ICC one of the reactions is specifically used for neurofibrillary tangles(NFT). ALZ-50 then is seen as an analogous, specifically for NFT, component of the double ICC being taught in the Ghanbari patent. Ghanbari et al. further teaches the advantage of using MC1 and TG-3 in addition to ALZ-50 as "ALZ-50 only reacts with the Alzheimer antigen, the TG-3 epitope can be generated on recombinant tau by appropriate phosphorylation, and its reactivity against the Alzheimer antigen is vastly greater than with phospho recombinant tau"(Col. 10, lines 2-7). The reference continues to teach that, "some recognize epitopes that are discontinuous (ALZ-50,

MC1), while others bind to epitopes that are both discontinuous and phosphorylation dependent(TG-3)"(Col. 10). The reference explains that for these reasons, "the lower reactivity of the antibodies with normal brain proteins is not problematic because a differential in antibody reactivity exists in AD due to the formation of the highly reactive Alzheimer antigen"(Col. 10, lines 15-19). In the end, as there exists a wide variety of monoclonal antibodies that are capable of staining the NFT when viewed under the microscope, the prospect of interchanging mAb69 for ALZ-50 in an ICC experiment would be a basic change to well established AD dogma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Markham et al. so as to have provided as step for determining the stage of Alzheimer's by obtaining neuronal cells and exposing at least one of the neuronal cells to two or more antibodies wherein the antibodies comprise: an anti-TG-3 and mAb69; or an anti-MC-1 and mAb69, as such a detection of NFT is standard protocol in evaluating AD ICC experiments and the use of such antibodies are typical of AD detection.

7. Claims 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al.(Neuroscience Letters, 1991) in view of Callahan et al. (Neurobiology of Aging, 1994) and in further view of Ghanbari et al. (US 5,811,310).

Allen et al. teach a method for creating a gene profile for a given stage of Alzheimer's disease by providing a plurality of "mRNAs found in a variety of extraneural tissues... because a hematogenous source for abnormal amyloid deposits is possible in AD"(Allen, 109). The reference teaches that forms of mRNA are present in human serum, plasma and platelets and often even in the cerebral vasculature. Determination of the level of mRNA expression is undertaken through either a method synthesizing cDNA by reverse transcription, or in the case of

some peripheral tissues, a RT-PCR method was employed. The reference teaches that the expression of mRNAs in AD-affected peripheral mononuclear blood cells(PMBCs), is relevant developmentally as they "give rise to microglia, which are often seen in proximity to Beta Amyloid Precursor Protein(BAPP) deposits"(109) eventually in the AD brain. The reference aptly teaches the detection of mRNA precursors to known components of the AD brain, as AD is a progressive neurodegenerative disorder characterized by abnormal deposition of the Beta amyloid protein(BAP).

Allen et al. do not teach determining the stage of Alzheimer's by obtaining neuronal cells and exposing at least one of the neuronal cells to two or more antibodies wherein the antibodies comprise: an anti-TG-3 and mAb69; or an anti-MC-1 and mAb69.

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However, Ghanbari et al. teach the use of an antibody, ALZ-50, whose action is analogous to that of mAb69 and whose action is taught to be coupled with the use of the claimed MC-1 and TG3. Ghanbari et al. teach that ALZ-50 reacts with normal and recombinant(abnormally phosphorylated) Tau from human origin. As is well known in the art, Ghanbari et al teach several antibodies that show reactivity to human tau either through non-specific cross-reactions with normal and abnormally phosphorylated tau or because they recognized specific epitopes on normal and abnormal phosphorylated tau. Ghanbari also reiterates that in the art many antibodies to specific phosphorylation sites and conformations of tau have been combined in double immunocytochemistry(ICC) experiments. It is further typical that in the ICC one of the reactions is specifically used for neurofibrillary tangles(NFT). ALZ-50 then is seen as an analogous, specifically for NFT, component of the double ICC being taught in the Ghanbari patent. Ghanbari et al. further teaches the advantage of using MC1 and TG-3 in addition to ALZ-50 as "ALZ-50 only reacts with the Alzheimer antigen, the TG-3 epitope can be generated on recombinant tau by appropriate phosphorylation, and its reactivity against the Alzheimer antigen is vastly greater than with phospho recombinant tau"(Col. 10, lines 2-7). The reference continues to teach that, "some recognize epitopes that are discontinuous (ALZ-50, MC1), while others bind to epitopes that are both discontinuous and phosphorylation dependent(TG-3)"(Col. 10). The reference explains that for these reasons, "the lower reactivity of the antibodies with normal brain proteins is not problematic because a differential in antibody reactivity exists in AD due to the formation of the highly reactive Alzheimer antigen"(Col. 10, lines 15-19). In the end, as there exists a wide variety of monoclonal antibodies that are capable

of staining the NFT when viewed under the microscope, the prospect of interchanging mAb69 for ALZ-50 in an ICC experiment would be a basic change to well established AD dogma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Allen et al. so as to have provided as step for determining the stage of Alzheimer's by obtaining neuronal cells and exposing at least one of the neuronal cells to two or more antibodies wherein the antibodies comprise: an anti-TG-3 and mAb69; or an anti-MC-1 and mAb69, as such a detection of NFT is standard protocol in evaluating AD ICC experiments and the use of such antibodies are typical of AD detection.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-65, 73-75, 87, 88, 90-92, and 99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "non-neural" stated specifically in claims 57, 75, 87, and 92 appears to represent new matter. The specification as originally filed

does not teach the concept of providing a plurality of cells from non-neural tissue. In applicant's supplemental Preliminary amendment filed in paper #8, applicant attempts to provide a reference illustrating the basis had in their specification for their newly added claims 57-100. Although applicant refers to page 18, lines 25-30, page 22, line 5 et seq, and page 35, lines 1-9, in an attempt to provide basis for the insertion of "non-neural tissues," they only successfully reveal basis for cells from a neural tissue, not all cells from the entire genus of both neural and non-neural tissues. Specifically, the exclusion proviso in which "non-neural" is distinguished is not found in the specification..

> "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

Since no basis has been identified, the claims are rejected as incorporating new matter.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-65, 73-75, 87, 88, 90-92, and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 57-65, 73-75, 87, 88, 90-92, and 99 are indefinite over the recitation of "non-neural tissue or bodily fluid." It is unclear from the specification what "non-neural" includes. It is unclear if "non-neural" requires that the tissue contain no neurons, that it not be found in the

brain, or alternatively if the tissue or bodily fluid can be found in the brain but just not contain neurons, or even if "non-neural" can include glial cells located in the tissue of the brain, etc. Applicant should amend the claims to clarify their intentions with respect to the non-neural tissue or bodily fluid being claimed.

B. Claims 87, 88, and 90-92 are indefinite. Claim 87... d). includes a method of comparing the product made by the method of claim 57, with an individual's and patient's profile. However, Claim 57 is a method claim, not a product claim. As a result, the method step in 87 d), of comparing an individual's and patient's profile to that profile which is created by the method of claim 57 is improper and should be amended as necessary to correct the improper dependency.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Thursday from 7:30AM-5:00PM and Friday from 1:00PM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703)308-1152. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

Sally Sakelaris

1/20/2003

CARLA J. MYERS
PRIMARY EXAMINER